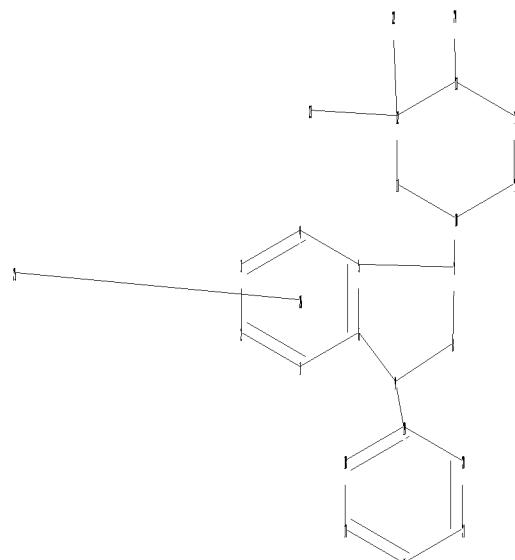
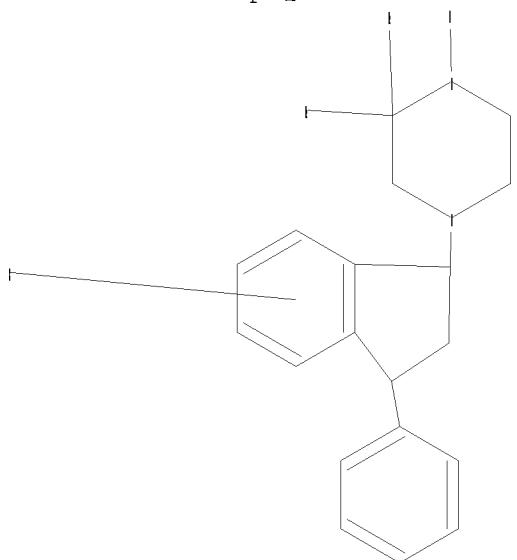


10/568292

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Uploading C:\Documents and Settings\EBernhardt\My Documents\Stnexp\Queries\10568292.str



chain nodes :

22 23 24 25

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

chain bonds :

7-10 9-19 12-22 12-23 13-24

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-15 11-12 12-13 13-14
14-15 16-17 16-21 17-18 18-19 19-20 20-21

exact/norm bonds :

5-7 6-9 7-8 7-10 8-9 10-11 10-15 11-12 12-13 13-14 14-15

exact bonds :

9-19 12-22 12-23 13-24

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-21 17-18 18-19 19-20 20-21

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:Atom

L1 STRUCTURE UPLOADED

=> s 11

SAMPLE SEARCH INITIATED 14:05:40 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 10 TO ITERATE

100.0% PROCESSED

10 ITERATIONS

2 ANSWERS

10/568292

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 11 TO 389
PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

=> s 11 sss full
FULL SEARCH INITIATED 14:05:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 140 TO ITERATE

100.0% PROCESSED 140 ITERATIONS 16 ANSWERS
SEARCH TIME: 00.00.01

L3 16 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
178.82 179.03

FILE 'CAPLUS' ENTERED AT 14:05:58 ON 03 MAY 2008
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE LAST UPDATED: 2 May 2008 (20080502/ED)

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They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s 13
L4 7 L3

=> d 14 1-7 bib abs hitstr

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:845656 CAPLUS
DN 145:271814
TI Crystalline base of trans-1-((1r,3s)-6-chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazine

IN Bang-Andersen, Benny; Lopez De Diego, Heidi

PA H. Lundbeck A/S, Den.

SO PCT Int. Appl., 30pp.

CODEN: PIXXD2

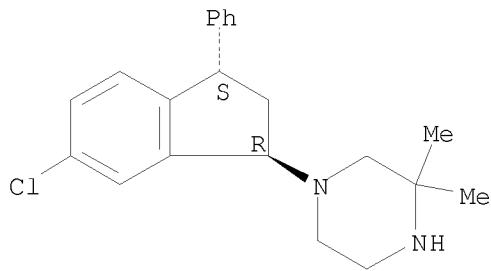
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006086986	A1	20060824	WO 2006-DK88	20060214
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	AU 2006215957	A1	20060824	AU 2006-215957	20060214
	CA 2597622	A1	20060824	CA 2006-2597622	20060214
	EP 1853576	A1	20071114	EP 2006-706059	20060214
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	KR 2007103414	A	20071023	KR 2007-717725	20070731
	CN 101119983	A	20080206	CN 2006-80005006	20070815
	MX 200709980	A	20070926	MX 2007-9980	20070816
	IN 2007CN03579	A	20071116	IN 2007-CN3579	20070816
	NO 2007004639	A	20070912	NO 2007-4639	20070912
PRAI	DK 2005-239	A	20050216		
	US 2005-653419P	P	20050216		
	WO 2006-DK88	W	20060214		
AB	Methods for preparing trans-1-(6-chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazine (I) are disclosed. The method involves resolution of racemic cis-6-chloro-3-phenylindan-1-ol which is dehydrated then undergoes substitution with 2,2-dimethylpiperazine to provide the free base I. Formation of salts of I are included. Further disclosed are pharmaceutical formulations.				
IT	846052-64-0P				
	RL: IMF (Industrial manufacture); PRP (Properties); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)				
	(crystal structure; process for preparation of tartrate and malate salts of trans-chlorophenylindanyl)dimethylpiperazine)				
RN	846052-64-0	CAPLUS			
CN	Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl- (CA INDEX NAME)				

Absolute stereochemistry.



IT 846052-66-2P 906665-78-9P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (process for preparation of tartrate and malate salts of
 trans-chlorophenylindanyl)dimethylpiperazine)

RN 846052-66-2 CAPLUS

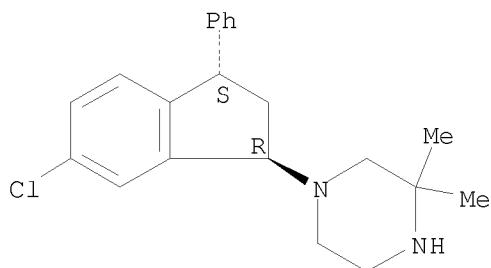
CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0

CMF C21 H25 Cl N2

Absolute stereochemistry.

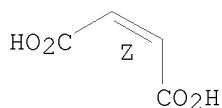


CM 2

CRN 110-16-7

CMF C4 H4 O4

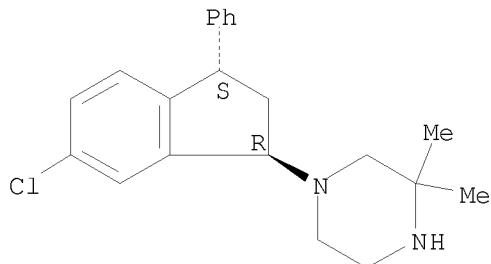
Double bond geometry as shown.



RN 906665-78-9 CAPLUS

CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, hydrochloride (1:?) (CA INDEX NAME)

Absolute stereochemistry.



● x HCl

IT 846052-73-1P 906665-81-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of tartrate and malate salts of
trans-chlorophenylindanyl)dimethylpiperazine)

RN 846052-73-1 CAPLUS

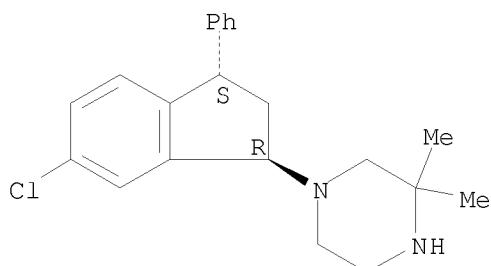
CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0

CMF C21 H25 Cl N2

Absolute stereochemistry.

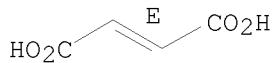


CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



RN 906665-81-4 CAPLUS

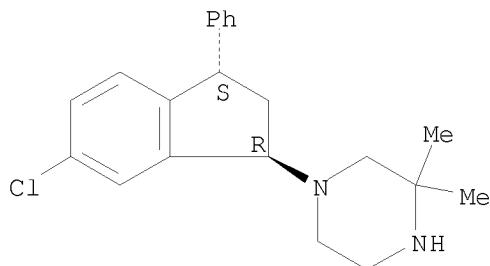
CN Butanedioic acid, compd. with 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethylpiperazine (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0

CMF C21 H25 Cl N2

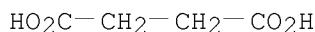
Absolute stereochemistry.



CM 2

CRN 110-15-6

CMF C4 H6 O4

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:845375 CAPLUS

DN 145:271813

TI Process for making trans-1-((1R,3S)-6-chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazine

IN Dahl, Allan, Carsten; Woehlk Nielsen, Christina; Suteu, Christina; Robin, David; Broesen, Peter

PA H. Lundbeck A/S, Den.

SO PCT Int. Appl., 39pp.

CODEN: PIXXD2

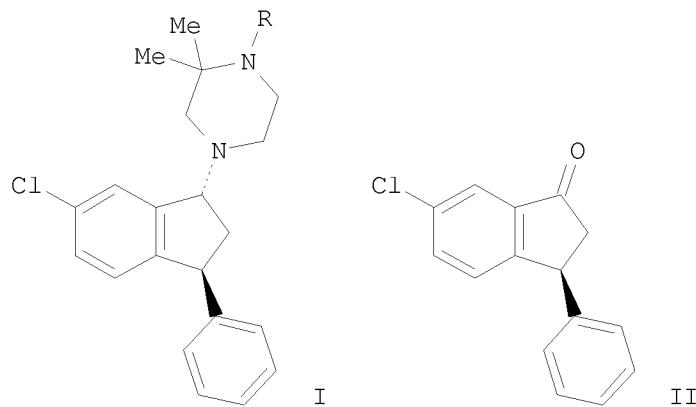
DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2006086984	A1	20060824	WO 2006-DK86	20060214

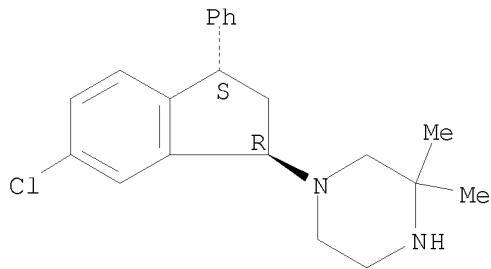
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RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
AU	2006215955	A1	20060824	AU	2006-215955	20060214
CA	2597615	A1	20060824	CA	2006-2597615	20060214
EP	1853574	A1	20071114	EP	2006-706057	20060214
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU					
KR	2007103386	A	20071023	KR	2007-716237	20070716
MX	200709814	A	20070907	MX	2007-9814	20070814
IN	2007CN03582	A	20071116	IN	2007-CN3582	20070816
CN	101137632	A	20080305	CN	2006-80005207	20070816
NO	2007004642	A	20070912	NO	2007-4642	20070912
PRAI	DK 2005-237	A	20050216			
	US 2005-653428P	P	20050216			
	WO 2006-DK86	W	20060214			
OS	CASREACT 145:271813;	MARPAT	145:271813			
GI						



AB Described is a method for making the trans-1-((1R,3S)-6-chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazine (I; R = H) and salts thereof and a similar method for making 4-((1R,3S)-6-chloro-3-phenylindan-1-yl)-1,2,2-trimethylpiperazine (I; R = Me) and salts thereof, which method comprises conversion of a compound of formula II to the compound of formula I.
IT 846052-64-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(process for making trans-(chlorophenylindanyl)dimethylpiperazine)
 RN 846052-64-0 CAPLUS
 CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

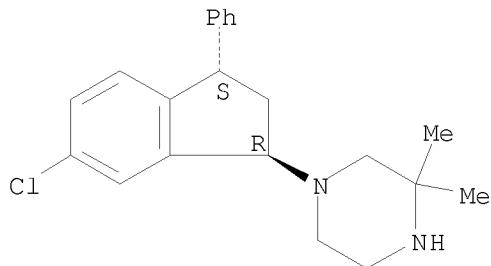


IT 846052-66-2P 846052-73-1P 906816-56-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (process for making trans-(chlorophenylindanyl)dimethylpiperazine)
 RN 846052-66-2 CAPLUS
 CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0
 CMF C21 H25 Cl N2

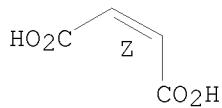
Absolute stereochemistry.



CM 2

CRN 110-16-7
 CMF C4 H4 O4

Double bond geometry as shown.



RN 846052-73-1 CAPLUS

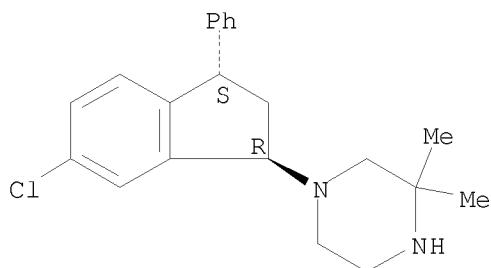
CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0

CMF C21 H25 Cl N2

Absolute stereochemistry.

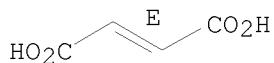


CM 2

CRN 110-17-8

CMF C4 H4 O4

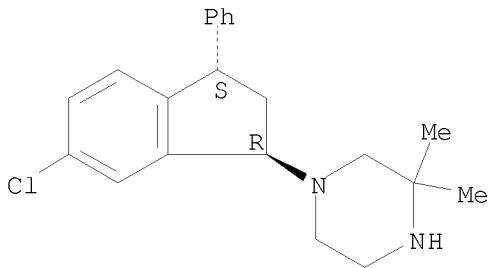
Double bond geometry as shown.



RN 906816-56-6 CAPLUS

CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:841777 CAPLUS
 DN 145:271805
 TI Process for preparation of tartrate and malate salts of
 trans-1-((1R,3S)-6-chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazine
 IN Nielsen, Ole; Lopez De Diego, Heidi; Bang-Andersen, Benny
 PA H. Lundbeck A/S, Den.
 SO PCT Int. Appl., 32pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006086985	A1	20060824	WO 2006-DK87	20060214
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	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU	2006215956	A1	20060824	AU 2006-215956	20060214
CA	2597620	A1	20060824	CA 2006-2597620	20060214
EP	1853575	A1	20071114	EP 2006-706058	20060214
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
MX	200709816	A	20070907	MX 2007-9816	20070814
KR	2007107043	A	20071106	KR 2007-718678	20070814
CN	101119982	A	20080206	CN 2006-80004964	20070815
IN	2007CN03581	A	20071116	IN 2007-CN3581	20070816

NO 2007004593	A 20070911	NO 2007-4593	20070911
PRAI DK 2005-238	A 20050216		
US 2005-653418P	P 20050216		
WO 2006-DK87	W 20060214		

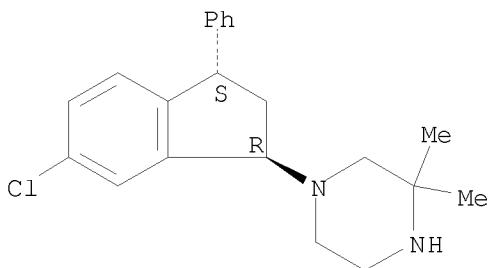
AB Methods for preparing tartrate and malate salts of trans-1-(6-chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazine (I) are disclosed. The method involves resolution of racemic cis-6-chloro-3-phenylindan-1-ol which is dehydrated then undergoes substitution with 2,2-dimethylpiperazine to provide the free base I. The salts of I are disclosed as useful for treatment of schizophrenia or other diseases involving psychotic symptoms. Further disclosed are pharmaceutical formulations.

IT 846052-64-0P
 RL: IMF (Industrial manufacture); PRP (Properties); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
 (crystal structure; process for preparation of tartrate and malate salts of trans-chlorophenylindanyl)dimethylpiperazine)

RN 846052-64-0 CAPLUS

CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 906665-80-3P
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
 (crystal structure; process for preparation of tartrate and malate salts of trans-chlorophenylindanyl)dimethylpiperazine)

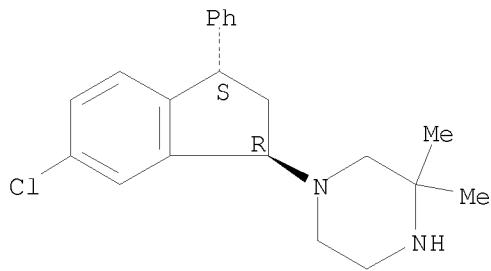
RN 906665-80-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethylpiperazine (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0
 CMF C21 H25 Cl N2

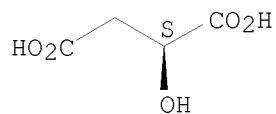
Absolute stereochemistry.



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 846052-66-2P 906665-78-9P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for preparation of tartrate and malate salts of trans-chlorophenylindanyl)dimethylpiperazine)

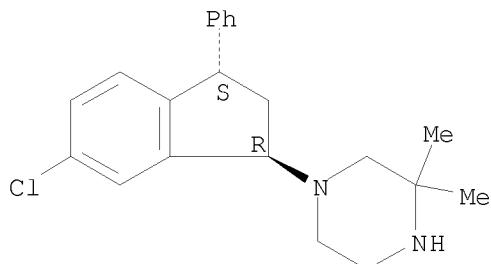
RN 846052-66-2 CAPLUS

CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0
CMF C21 H25 Cl N2

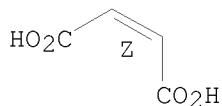
Absolute stereochemistry.



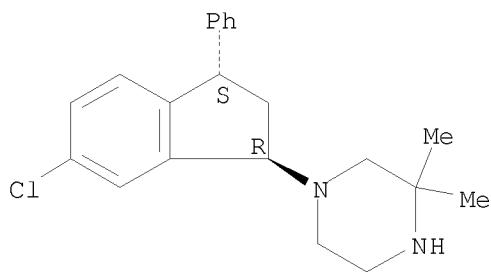
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

RN 906665-78-9 CAPLUS
CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, hydrochloride (1:?) (CA INDEX NAME)

Absolute stereochemistry.



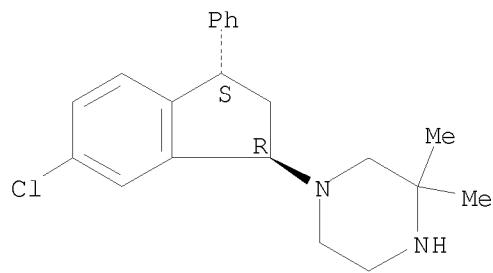
● x HCl

IT 846052-73-1P 906665-79-0P 906665-81-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of tartrate and malate salts of
trans-chlorophenylindanyl)dimethylpiperazine)
RN 846052-73-1 CAPLUS
CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0
CMF C21 H25 Cl N2

Absolute stereochemistry.

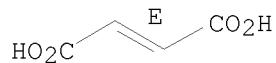


CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



RN 906665-79-0 CAPLUS

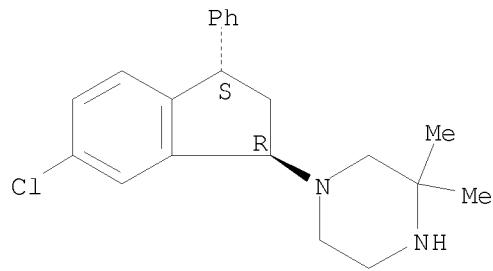
CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0

CMF C21 H25 Cl N2

Absolute stereochemistry.

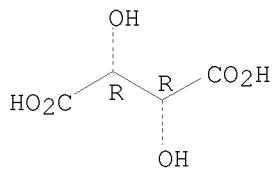


CM 2

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.



RN 906665-81-4 CAPLUS

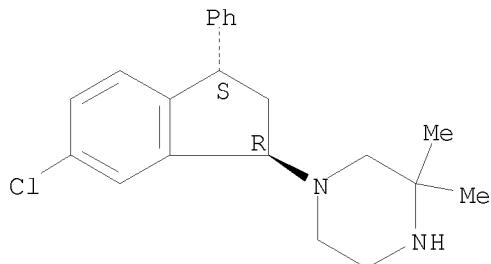
CN Butanedioic acid, compd. with 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethylpiperazine (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0

CMF C21 H25 Cl N2

Absolute stereochemistry.



CM 2

CRN 110-15-6

CMF C4 H6 O4

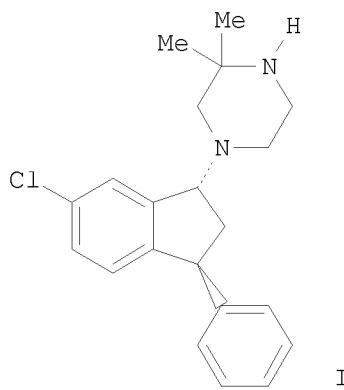
HO₂C—CH₂—CH₂—CO₂HRE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:158652 CAPLUS
 DN 142:261559
 TI trans-1-(6-Chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazine enantiomer and salts, and their preparation, pharmaceutical compositions, and use, particularly as antipsychotics
 IN Bang-Andersen, Benny; Bogeso, Klaus Peter; Jensen, Klaus Gjervig; Svane, Henrik; Dahl, Allan Carsten; Howells, Mark; Lyngso, Lars Ole; Mow, Tomas H. Lundbeck A/S, Den.
 PA PCT Int. Appl., 38 pp.
 SO CODEN: PIXXD2
 DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005016901	A1	20050224	WO 2004-DK546	20040818
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004265022	A1	20050224	AU 2004-265022	20040818
	CA 2536073	A1	20050224	CA 2004-2536073	20040818
	EP 1658276	A1	20060524	EP 2004-739041	20040818
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1835938	A	20060920	CN 2004-80023638	20040818
	BR 2004013555	A	20061017	BR 2004-13555	20040818
	JP 2007502784	T	20070215	JP 2006-523529	20040818
	IN 2006CN00566	A	20070622	IN 2006-CN566	20060215
	MX 2006PA01938	A	20060517	MX 2006-PA1938	20060217
	NO 2006001153	A	20060310	NO 2006-1153	20060310
	US 20060281758	A1	20061214	US 2006-568292	20060814
PRAI	DK 2003-1180	A	20030818		
	US 2003-496058P	P	20030818		
	DK 2003-1305	A	20030911		
	US 2003-520246P	P	20031114		
	WO 2004-DK546	W	20040818		
OS	MARPAT 142:261559				
GI					



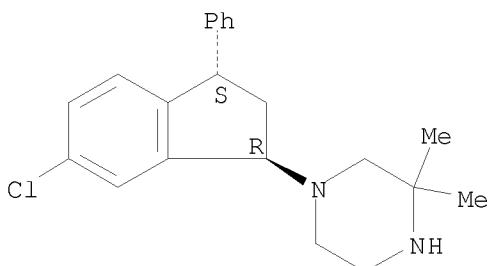
AB The compound 4-((1R,3S)-6-chloro-3-phenylindan-1-yl)-2,2-dimethylpiperazine

(I) and salts are disclosed. Also disclosed are pharmaceutical compns. comprising I and salts, and their medical uses, including those for the treatment of schizophrenia and other psychotic disorders. The biol. activity of I and salts is described and discussed (no data). I displays a high affinity for dopamine D1 receptors, dopamine D2 receptors, and for $\alpha 1$ adrenoceptors. Furthermore, I is an antagonist at dopamine D1 and D2 receptors, and at serotonin 5-HT2A receptors. The pharmacol. activities of I are, with respect to these receptors, similar to those of the analogous compound having a Me group instead of a hydrogen on the piperazine. The racemate of I is also considerably more potent on the CYP2D6 enzyme compared to the enantiomer of the invention, i.e., I. The fact that I has a low interaction with the liver enzyme CYP2D6 means that it has a reduced potential for drug-drug interaction, i.e., there is possibly less drug-drug interaction when a patient is treated with I together with other drugs which are mainly metabolized by the CYP2D6 enzyme. This is a considerable advantage, in particular for patients with schizophrenia, who are often treated with other medicaments to control their disease. I also has a relatively low prolonging effect on the QT-interval in the ECG of the "alpha-chloroanesthetized rabbit". The fact that I has a relatively low effect on the rabbit QT interval means that this compound has a reduced potential for introducing drug-induced QT interval prolongation and appearance of fatal cardiac arrhythmias, torsade de pointes (TdP), in humans, compared to several com. antipsychotics. For example, racemic cis-6-chloro-3-phenylindan-1-ol was resolved by chiral chromatog. or enzymic resolution to give the (+)-(1S,3S) isomer, which was chlorinated with SOCl_2 and then aminated with 2,2-dimethylpiperazine, to give I as a cis/trans mixture. Conversion of the free base of I to the hydrogen maleate salt by precipitation with maleic acid gave I maleate with no detectable cis isomer, and enantiomeric excess (ee) being >99%.

IT 846052-64-0P, trans-1-((1R,3S)-6-Chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazine 846052-66-2P, trans-1-((1R,3S)-6-Chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazinium hydrogen maleate
 846052-73-1P, trans-1-((1R,3S)-6-Chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazinium fumarate 846052-78-6P, trans-1-(6-Chloro-3-phenylindan-1-yl)-3,3-dimethylpiperazine
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (drug candidate; preparation of (chlorophenylindanyl)dimethylpiperazine enantiomer and salts as antipsychotics)

RN 846052-64-0 CAPLUS
 CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.



10/568292

RN 846052-66-2 CAPLUS

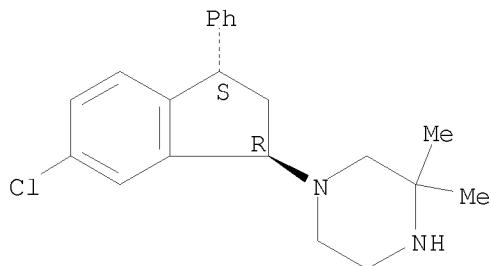
CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0

CMF C21 H25 Cl N2

Absolute stereochemistry.

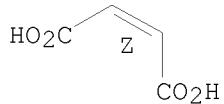


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



RN 846052-73-1 CAPLUS

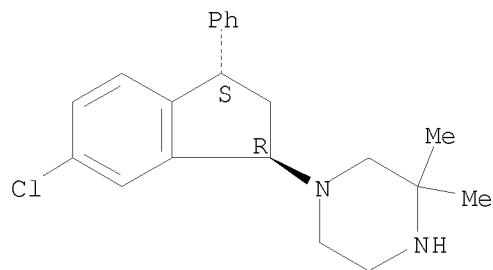
CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0

CMF C21 H25 Cl N2

Absolute stereochemistry.

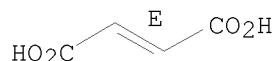


CM 2

CRN 110-17-8

CMF C4 H4 O4

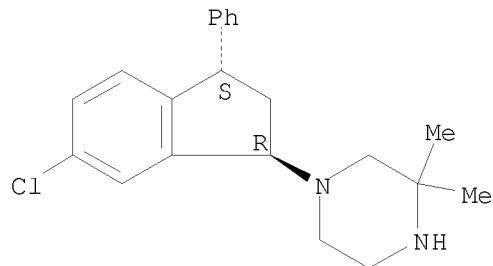
Double bond geometry as shown.



RN 846052-78-6 CAPLUS

CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, rel- (CA INDEX NAME)

Relative stereochemistry.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:158651 CAPLUS

DN 142:261558

TI Succinate and malonate salts of trans-4-(1R,3S)-6-chloro-3-phenylindan-1-yl)-1,2,2-trimethylpiperazine and their preparation, pharmaceutical compositions, and use as medicaments, particularly as antipsychotics

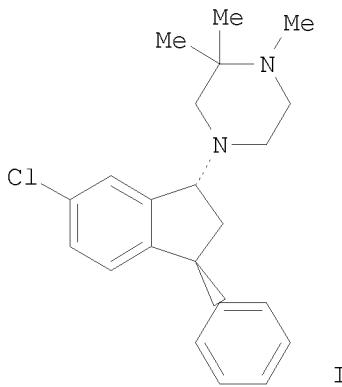
IN Lopez De Diego, Heidi; Nielsen, Ole; Ringgard, Lone Munch; Svane, Henrik; Dahl, Allan Carsten; Howells, Mark; Bang-Andersen, Benny

PA H. Lundbeck A/S, Den.

SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2

DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005016900	A1	20050224	WO 2004-DK545	20040818
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004265021	A1	20050224	AU 2004-265021	20040818
	CA 2536144	A1	20050224	CA 2004-2536144	20040818
	EP 1658277	A1	20060524	EP 2004-762772	20040818
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1839124	A	20060927	CN 2004-80023725	20040818
	BR 2004013595	A	20061017	BR 2004-13595	20040818
	JP 2007502783	T	20070215	JP 2006-523528	20040818
	IN 2006CN00557	A	20070622	IN 2006-CN557	20060215
	MX 2006PA01838	A	20060504	MX 2006-PA1838	20060216
	NO 2006001151	A	20060310	NO 2006-1151	20060310
	US 20060281759	A1	20061214	US 2006-568572	20060814
PRAI	DK 2003-1180	A	20030818		
	US 2003-496058P	P	20030818		
	DK 2003-1305	A	20030911		
	US 2003-520246P	P	20031114		
	WO 2004-DK545	W	20040818		
OS	CASREACT 142:261558; MARPAT 142:261558				
GI					



AB The salts 4-((1R,3S)-6-chloro-3-phenylindan-1-yl)-1,2,2-trimethylpiperazine (I) hydrogen succinate and hydrogen malonate are

disclosed. Also disclosed are pharmaceutical compns. containing these salts, and their medical uses, including those for the treatment of schizophrenia and other psychotic disorders. Also described are methods for the preparation of I, and medical uses thereof. I, which has been previously described, is a mixed D1/D2 antagonist and a 5-HT2 antagonist, with an affinity for $\alpha 1$ adrenoceptors as well. The fumarate salt of I has also been described. The invention salts (hydrogen succinate and hydrogen malonate) show a considerably larger aqueous solubility than does the fumarate. The invention salts also show favorable stability and non-hygroscopicity. Two crystalline forms of the hydrogen succinate were observed. The salts are expected

to show the same general utility as I toward a variety of CNS disease states (no data). The 5-HT2 antagonistic activity of the salts suggest a relatively low risk of extrapyramidal side effects. For example, racemic cis-6-chloro-3-phenylindan-1-ol was resolved by chiral chromatog. or enzymic resolution to give the (+)-(1S,3S) isomer, which was chlorinated with SOCl_2 and then aminated with 1,2,2-trimethylpiperazine, to give I as a cis/trans mixture. Conversion of the ee base of I to the hydrogen fumarate salt by precipitation with fumaric acid gave I fumarate with no detectable cis isomer. This stereochem. pure salt was converted back to the ee base of I with aqueous NH_3 , followed by extraction into PhMe , evaporation, and conversion to the

hydrogen succinate by precipitation on acetone. The initially formed succinate was the beta form, but repetitions of the procedure gave the more stable alpha form. In water at room temperature, I salts had the following solubilities: alpha (1:1) succinate 13, (1:1) malonate 15, and fumarate 1.5 mg/mL. The new salts, and particularly the succinate, showed better overall heat and light stability relative to the fumarate.

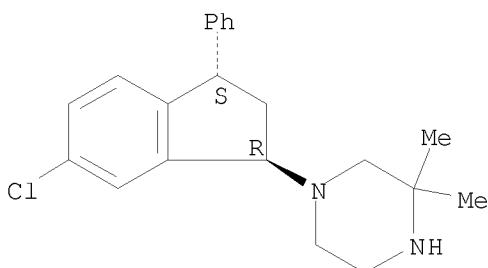
IT 846052-64-0P, trans-1-[(1R,3S)-6-Chloro-3-phenylindan-1-yl]-3,3-dimethylpiperazine

RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent (intermediate; preparation of succinate and malonate salts of (chlorophenylindanyl)trimethylpiperazine as antipsychotics)

RN 846052-64-0 CAPLUS

CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.



IT 846052-73-1P, trans-1-[(1R,3S)-6-Chloro-3-phenylindan-1-yl]-3,3-dimethylpiperazine hydrogen fumarate

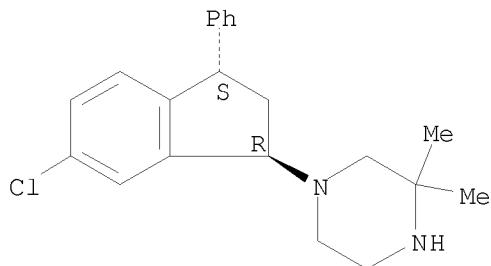
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation) (intermediate; preparation of succinate and malonate salts of

(chlorophenylindanyl)trimethylpiperazine as antipsychotics)
 RN 846052-73-1 CAPLUS
 CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0
 CMF C21 H25 Cl N2

Absolute stereochemistry.



CM 2

CRN 110-17-8
 CMF C4 H4 O4

Double bond geometry as shown.

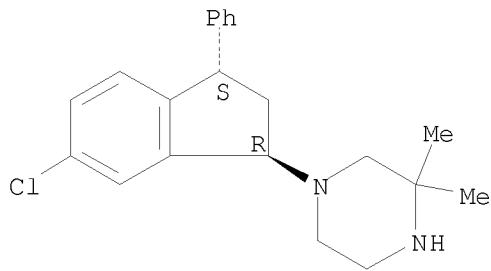


IT 846052-66-2P, trans-1-[(1R,3S)-6-Chloro-3-phenylindan-1-yl]-3,3-dimethylpiperazine hydrogen maleate
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of succinate and malonate salts of (chlorophenylindanyl)trimethylpiperazine as antipsychotics)
 RN 846052-66-2 CAPLUS
 CN Piperazine, 1-[(1R,3S)-6-chloro-2,3-dihydro-3-phenyl-1H-inden-1-yl]-3,3-dimethyl-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 846052-64-0
 CMF C21 H25 Cl N2

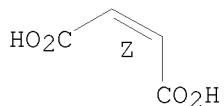
Absolute stereochemistry.



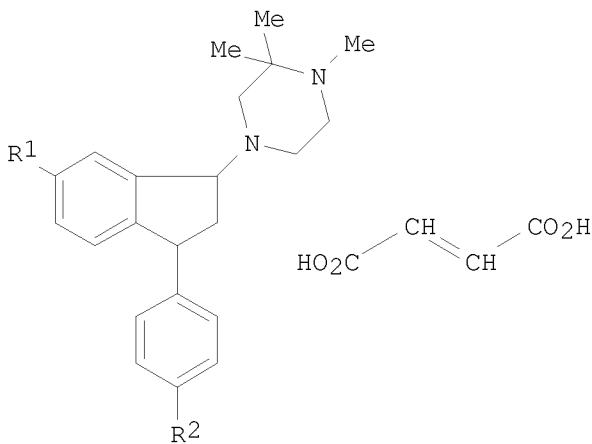
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 1995:849924 CAPLUS
 DN 123:329244
 TI Enhanced D1 Affinity in a Series of Piperazine Ring Substituted
 1-Piperazino-3-Arylindans with Potential Atypical Antipsychotic Activity
 AU Bogeso, Klaus P.; Arnt, Jorn; Frederiksen, Kristen; Hansen, Hans Otto;
 Hyttel, John; Pedersen, Henrik
 CS Research Development H. Lundbeck A/S, Copenhagen, DK-2500, Den.
 SO Journal of Medicinal Chemistry (1995), 38(22), 4380-92
 CODEN: JMCMAR; ISSN: 0022-2623
 PB American Chemical Society
 DT Journal
 LA English
 GI



I R¹ = Cl, R² = H

II R¹ = F, R² = F

AB A study of the effect of aromatic substitution on D1 and D2 affinity in a series of previously reported trans-1-piperazino-3-phenylindans shows similar structure-activity relationships for the two receptor sites. 6-Substituted derivs. have affinity for both receptors, and 6-chloro- or 6-fluoro-substituted derivs. show preference for D1 receptors. D1 affinity and selectivity are significantly increased in a series of new piperazine ring substituted derivs. Potent D1 and D2 antagonism *in vivo* are confined to derivs. with relatively small substituents in the 2-position of the piperazine ring (e.g. 2-Me, 2,2-di-Me, 2-spirocyclobutyl or 2-spirocyclopentyl). Consequently, the effect of aromatic substitution is examined in a series of 1-(2,2-dimethylpiperazino)-3-aryllindans. All these compds. except the 4-, 5-, 7- and 4'-chloro-substituted derivs. have potent D1 affinity (IC₅₀'s below 10 nM) and the majority of the compds. antagonize SK&F 38393-induced circling in 6-OHDA-lesioned rats with ED₅₀ values about 1 μ mol/kg. In vitro all compds. show preference for D1 receptors, but *in vivo* they are equally effective as D1 and D2 antagonists. The compds. have high affinity for 5-HT₂ receptors and selected compds. show high affinity for α 1-adrenoceptors. Furthermore, some of the tested compds. do not induce catalepsy in rats. These compds. have the potential of being "atypical" antipsychotics and have consequently been selected for further studies. The non-receptor-blocking enantiomers are shown to be inhibitors of DA and NE uptake in accordance with previous observations in compds. unsubstituted in the piperazine ring. Two compds., I and II, block DA uptake with IC₅₀ values below 10 nM. Finally, the observed structure-activity relationships are discussed in relation to previously published pharmacophore models for D2 and 5-HT₂ receptors. It is concluded that the piperazine substituents might induce a different binding mode at the dopamine receptor sites, perhaps only at the D1 receptor site.

IT 153626-87-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(enhanced D1 affinity in a series of piperazine ring substituted 1-piperazino-3-aryllindans with potential atypical antipsychotic

activity)

RN 153626-87-0 CAPLUS

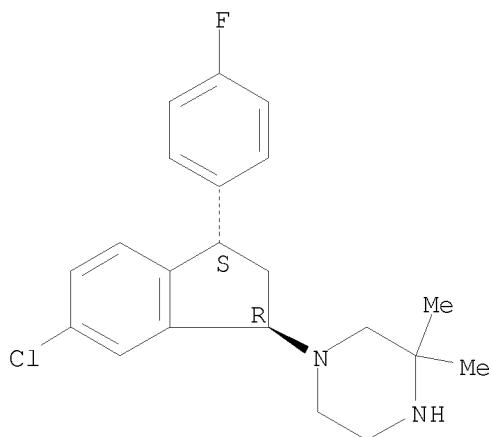
CN Piperazine, 1-[(1R,3S)-6-chloro-3-(4-fluorophenyl)-2,3-dihydro-1H-inden-1-yl]-3,3-dimethyl-, rel-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 153626-86-9

CMF C21 H24 Cl F N2

Relative stereochemistry.

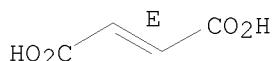


CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



IT 153626-87-0P 170381-33-6P 170381-35-8P

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (structure activity relations in D1- and D2-dopaminergic receptor affinity of piperazinoarylindans)

RN 153626-87-0 CAPLUS

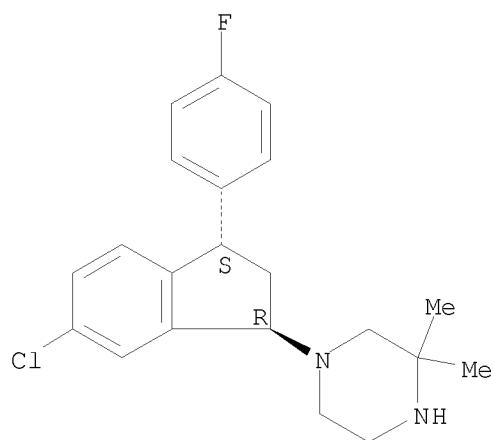
CN Piperazine, 1-[(1R,3S)-6-chloro-3-(4-fluorophenyl)-2,3-dihydro-1H-inden-1-yl]-3,3-dimethyl-, rel-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 153626-86-9

CMF C21 H24 Cl F N2

Relative stereochemistry.



CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



RN 170381-33-6 CAPLUS

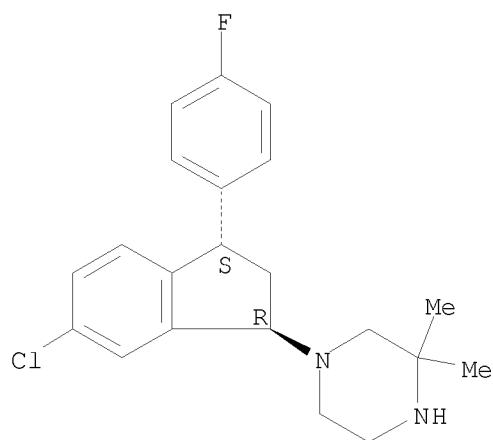
CN Piperazine, 1-[(1R,3S)-6-chloro-3-(4-fluorophenyl)-2,3-dihydro-1H-inden-1-yl]-3,3-dimethyl-, rel-(-)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 170381-32-5

CMF C21 H24 Cl F N2

Rotation (-). Absolute stereochemistry unknown.



CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



RN 170381-35-8 CAPLUS

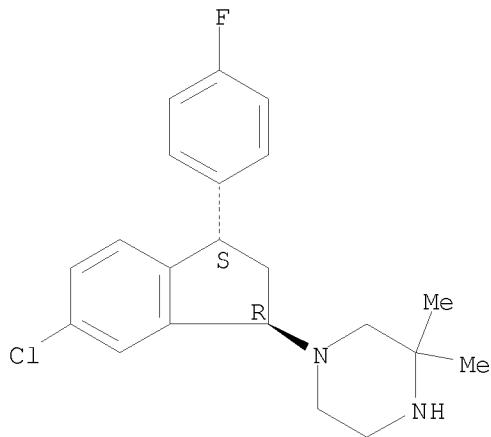
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CM 1

CRN 170381-34-7

CMF C21 H24 Cl F N2

Rotation (+). Absolute stereochemistry unknown.

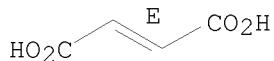


CM 2

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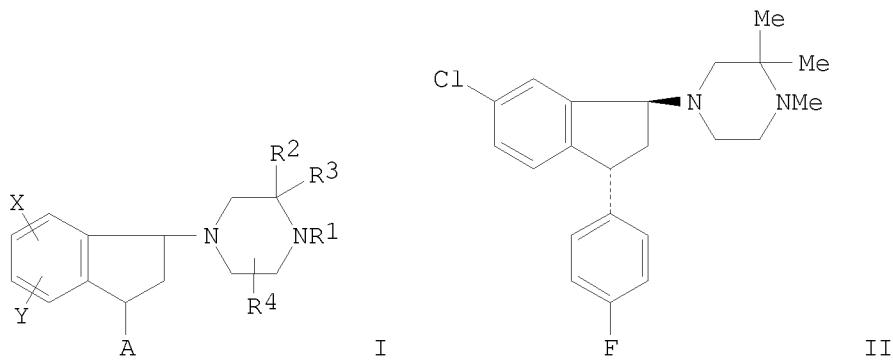
Double bond geometry as shown.



L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 1994:191735 CAPLUS
 DN 120:191735
 TI 1-piperazino-1,2-dihydroindene derivatives
 IN Boegesoe, Klaus; Bregnedal, Peter
 PA Lundbeck, H. a/s, Den.
 SO PCT Int. Appl., 33 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9322293	A1	19931111	WO 1993-DK136	19930423
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	IL 105464	A	19980104	IL 1993-105464	19930420
	ZA 9302840	A	19931123	ZA 1993-2840	19930422
	AU 9340599	A	19931129	AU 1993-40599	19930423
	AU 669709	B2	19960620		
	EP 638073	A1	19950215	EP 1993-909807	19930423
	EP 638073	B1	20000621		
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JP 07505895	T 19950629	JP 1993-518845	19930423
JP 3255416	B2 20020212		
HU 71419	A2 19951128	HU 1994-3098	19930423
CZ 281676	B6 19961211	CZ 1994-2619	19930423
RU 2114106	C1 19980627	RU 1994-45948	19930423
AT 194003	T 20000715	AT 1993-909807	19930423
ES 2148227	T3 20001016	ES 1993-909807	19930423
PT 638073	T 20001130	PT 1993-909807	19930423
SK 281613	B6 20010510	SK 1994-1293	19930423
CA 2134566	C 20040810	CA 1993-2134566	19930423
FI 9405042	A 19941026	FI 1994-5042	19941026
FI 113862	B1 20040630		
NO 9404090	A 19941220	NO 1994-4090	19941027
NO 306946	B1 20000117		
US 5807855	A 19980915	US 1994-331213	19941028
HK 1013816	A1 20001201	HK 1998-115090	19981223
GR 3034396	T3 20001229	GR 2000-402086	20000913
PRAI DK 1992-551	A 19920428		
WO 1993-DK136	A 19930423		
OS MARPAT 120:191735			
GI			



AB Trans-isomers of 1-piperazino-1,2-dihydroindene compds. having general formula I (R1-R4 = H, alkyl, etc.; X, Y = H, halo, etc.; A = Ph, etc.) and their uses as potential antagonists of D1 receptors are claimed. The compds. are useful in the treatment of diseases in the central nervous system, in particular psychosis, schizophrenia (pos. as well as neg. symptoms), anxiety, depression, sleep disturbances, migraine, Parkinson's disease or cocaine abuse. An example compound, (\pm)-trans-4-[6-chloro-3-(4-fluorophenyl)-2,3-dihydro-1H-inden-1-yl]-1,2,2-dimethylpiperazine (II) was prepared. The activity of II as D1, D2 and 5-HT2 receptor antagonists was tested.

IT 153626-87-0 153627-14-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as dopamine D1 antagonist)

RN 153626-87-0 CAPLUS

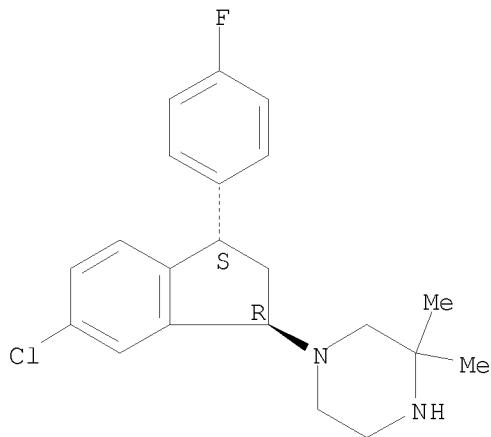
CN Piperazine, 1-[(1R,3S)-6-chloro-3-(4-fluorophenyl)-2,3-dihydro-1H-inden-1-yl]-3,3-dimethyl-, rel-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

10/568292

CM 1

CRN 153626-86-9
CMF C21 H24 Cl F N2

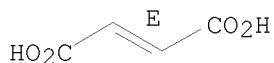
Relative stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

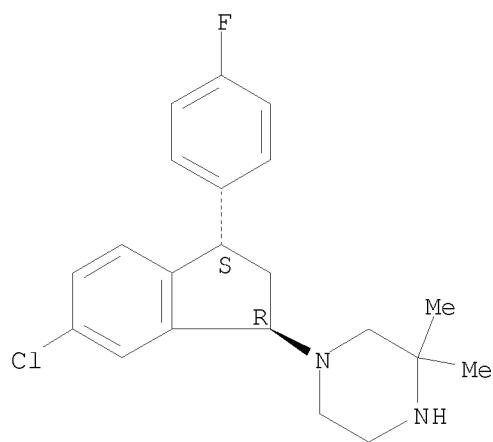


RN 153627-14-6 CAPLUS
CN Piperazine, 1-[(1R,3S)-6-chloro-3-(4-fluorophenyl)-2,3-dihydro-1H-inden-1-yl]-3,3-dimethyl-, rel-, (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 153626-86-9
CMF C21 H24 Cl F N2

Relative stereochemistry.

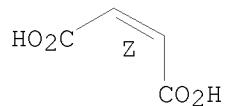


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



IT 153626-86-9

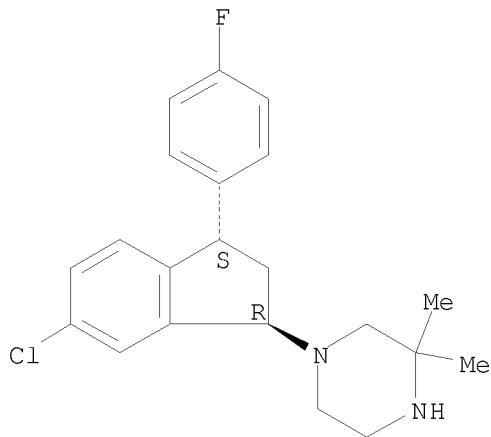
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation as intermediate for trans-(piperazino)dihydroindene dopamine D1 antagonist)

RN 153626-86-9 CAPLUS

CN Piperazine, 1-[6-chloro-3-(4-fluorophenyl)-2,3-dihydro-1H-inden-1-yl]-3,3-dimethyl-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



```

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FULL ESTIMATED COST          39.11        218.14

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE      TOTAL
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10/568292

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